DETAILED ACTION

Election/Restrictions

Applicant's election of Group XI, drawn to a vector system comprising a vector encoding a capsid protein and a vector comprising the BAAV ITR's, in the reply filed on 11/15/2010 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

In the reply, applicant canceled all previously pending claims and submitted new claims 112-150. New claim 112, for example, recites various SEQ ID NOs not found in the original claims.

Claim(s) 112-150 is/are generic to the following disclosed patentably distinct species: the different species of capsid proteins recited in claim 112(b), for example, and represented by SEQ ID NOs 7, 9 and 11. The species are independent or distinct because they are mutually exclusive amino acid or nucleic acid sequences. In addition, these species are not obvious variants of each other based on the current record.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species, or a single grouping of patentably indistinct species, for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

There is a search and/or examination burden for the patentably distinct species as set forth above because at least the following reason(s) apply:

1) the inventions have acquired a separate status in the art in view of their different classification;

2) the inventions have acquired a separate status in the art due to their recognized divergent subject matter;

3) the inventions require a different field of search (e.g., searching different classes /subclasses or electronic resources, or employing different search strategies or search queries).

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or a grouping of patentably indistinct species to be examined even though the requirement may be traversed (37 CFR 1.143) **and (ii) identification of the claims encompassing the elected species or grouping of patentably indistinct species**, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

The election may be made with or without traverse. To preserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the election of species requirement, the election shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable on the elected species or grouping of patentably indistinct species.

Should applicant traverse on the ground that the species, or groupings of patentably indistinct species from which election is required, are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing them to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the species unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other species.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141.

A telephone call was made to Richard Stern on 12/17/2010 to request an oral election to the above restriction requirement. Applicants elected SEQ ID NO: 11.

Claims 122, 123, 125, and 141-144 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 11/15/2010.

Specification

Sequence Rules

Figures 1-3 sequences not identified by a SEQ ID number in the figures themselves or in the Brief Description of the Drawings. Although these sequences appear to be found in the sequence listing, they must also be identified in the figures or the description of the drawings using the SEQ ID NO.

These details are requirements of the Sequence Rules (MPEP 2400 §1.821-1.825) and must be corrected. Any response which does not include compliance with the Sequence Rules will be considered non-responsive.

Claim Objections

Claims 112 and 131 (and all dependent claims) are objected to because of the following informalities: they recite non-elected subject matter, i.e. they recite part (c) in claim 112. As

currently worded, the claims do not require either of the elected components of the invention, i.e. parts (a) and (b). If applicants would like to include the subject matter of claim 112, part (c), the scope of claim 145 is suggested, i.e. the use of the conjunction "and" to link the required components. Appropriate correction is required.

Information Disclosure Statement

The information disclosure statement filed 6/2/2006 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

It is noted applicants cite MPEP 1893.03(g) as evidence that submission of the documents is not required. A reading of this section reveals nothing to support this, rather:

> "The examiner will consider the documents cited in the international search report, without any further action by applicant under 37 CFR 1.97 and 1.98, when both the international search report and copies of the documents are indicated to be present in the national stage file."

A review of the PCT/DO/EO/903 form dated 12/21/2006 reveals that no copies of the documents were received in this application, although the international search report has been made of record.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 112-114, 116-118, 126-130 are rejected under 35 U.S.C. 102(b) as being anticipated by Chiorini et al (WO 99/61601, 1999).

Chiorini et al teach AAV5 vectors comprising two AAV5 ITR's, which are 95% identical to instant SEQ ID NO: 12, see for example, Fig. 4 of Chiorini et al, residues 4505-4652 (7 mismatches of the 150 base pairs found in SEQ ID NO: 12). One AAV5 ITR has instant SEQ ID NO: 14 at residues 4502-4508, and thus comprises the TRS recited in the instant claims. The limitations of instant claims 126-130 are found in claims 1-7 of Chiorini et al.

Claims 112 and 120 are rejected under 35 U.S.C. 102(e) as being anticipated by Arbetman et al (US 7,259,151, e.f.d. 6/19/2003).

Arbetman et al disclose a protein (SEQ ID NO: 26) and nucleic acid (SEQ ID NO: 25) that are each 99% identical to instant SEQ ID NO: 11 and SEQ ID NO: 10, respectively.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 112-118, 120, 126-140, and 145-150 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compositions comprising the BAAV ITR and capsid protein set forth in SEQ ID NOs: 12 and 10, respectively, does not reasonably provide enablement for other BAAV ITRs, capsid proteins, or variants thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Claims 112-118, 120, 126-140, and 145-150 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

While the written description and enablement requirements are separate and generally separable requirements, the instant application fails to meet either requirement for essentially the same reasons, as set forth below.

Applicants claim vectors comprising BAAV ITRs, nucleic acids encoding BAAV VP3 (SEQ ID NO: 11), or variants thereof (e.g. 95% identity as found in claim 112). Applicants disclose a single sequence (i.e. SEQ ID NO:12 as a BAAV ITR and SEQ ID NO: 11 as VP3) for each vector component, isolated from a cloned BAAV. The claims read on a broad genus of BAAV ITR sequences (not limited to any particular nucleic acid sequence), BAAV VP3

sequences, and variants, such as any sequence that could be considered a "BAAV ITR" (which includes known AAV ITR sequences, see above, or any nucleic acid sequence with as little as 60% homology to SEQ ID NO: 12, see claim 116), or any amino acid sequence with 95% homology to SEQ ID NO: 11.

The written description requirement for a genus may be satisfied by sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function, or by a combination of such identifying characteristics, sufficient to show that applicant was in possession of the claimed invention. The court and the Board have repeatedly held (Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.,18 USPQ2d 1016 (CA FC, 1991); Fiers v. Revel, 25 USPQ2d 1601 (CA FC 1993); Fiddes v. Baird, 30 USPQ2d 1481 (BPAI 1993) and Regents of the Univ. Calif. v. Eli Lilly & Co., 43 USPQ2d 1398 (CA FC, 1997)) that an adequate written description of a nucleic acid or protein requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it, irrespective of the complexity or simplicity of the method; what is required is a description of the nucleic acid or protein itself. It is not sufficient to define DNA solely by its principal biological property, because disclosure of no more than that, as in the instant case, is simply a wish to know the identity of any DNA with that biological property. Naming a type of material generically known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. When one is unable to envision the detailed constitution of a complex chemical compound having a particular function, such as a nucleic acid or protein, so as to distinguish it

from other materials, as well as a method for obtaining it, conception has not been achieved until reduction to practice has occurred, i.e., until after the nucleic acid has been isolated. Thus, claiming all DNA's that achieve a result without defining what means will do so is not in compliance with the description requirement. Rather, it is an attempt to preempt the future before it has arrived. Also, where a claim purports to cover all nucleic acids that encode a specific protein and the specification discloses but a single DNA known to do so, the situation is analogous to a single means claim and does not meet the enablement requirement under para. 1 of §112. The court has also held that a claimed nucleic acid could meet the written description and enablement requirements if the nucleic acid were defined by a disclosed process found, after-the-fact, to produce the nucleic acid, and claimed as a product-by-process. However, in the instant case, the nucleic acids are not claimed as a product-by-process, nor does the specification disclose any process known to yield a claimed nucleic acid.

In terms of the structural requirements of the nucleic acid and protein molecules, claims 112, 116-118, 120, 131, and the like recite an arbitrary structural relationship between the claimed nucleic acid and protein sequence(s) and the single disclosed species of nucleotide sequence and amino acid sequence, respectively, based upon homology of the nucleic acids and/or protein sequence. The recited structural relationship for the claimed "BAAV ITR" is arbitrary since neither the specification nor the prior art discloses any definitive relationship between the claimed nucleic acid function as an ITR and % identity or homology at the nucleotide level; and the specification does not describe a single species of nucleic acid that meets the claim requirements that is not either 100% identical to SEQ ID NO: 12 (or that encodes a polypeptide that is not 100% identical to SEQ ID NO: 11).

While one of skill in the art can readily envision numerable species of nucleic acid or protein sequences that are at least a given % identity to a reference sequence and that encode a polypeptide at least a given % identity to a recited reference amino acid sequence, one cannot envision which of these also encode a polypeptide with a specified activity. The fact remains that the actual nucleic acid sequences which encode a protein with a particular activity or the actual amino acid sequences of such a protein cannot be envisioned any better when the possible choices are narrowed from all possible sequences to all possible sequences with an arbitrary structural relationship with a known functional sequence. For example, if one skilled in the art were to make a synthetic nucleotide sequence that encoded a polypeptide with 95% identity to the reference sequence, he would be no more able to say whether it encoded a BAAV ITR or VP3 than if the nucleotide sequence encoded a sequence that was only 10% identical to the reference polypeptide sequence. Nor would he be able to say whether the sequence existed in nature.

In the instant case, applicants only disclose the BAAV ITR and VP3 from a single BAAV isolate (i.e. the amino acid sequence of SEQ ID NO: 11 and ITR sequence of SEQ ID NO: 12). Neither applicants nor the prior art disclose other BAAV ITRs, yet the ITR from AAV5 is 95% similar. How then could the skilled artisan determine if they are using a "BAAV ITR" or an "AAV5 ITR"? It is not clear whether ITRs from other sources are included in the scope of claim 112, for instance, due to the broad nature of the claim. Applicants are claiming other forms of BAAV ITRs, VP3 proteins, and associated variants, by function only, without a correlation between structure and function. Applicants provide no disclosure of what structural feature(s) of the instantly disclosed BAAV ITRs or VP3 are responsible for the observed characterization as

"BAAV" relative to other known AAV sequences. Given the diversity of the claimed VP3 and ITR variants, it is incumbent upon the specification to disclose means for identifying such protein and nucleic acid variants commensurate in scope with coverage sought by the claims. The diversity of the VP3 proteins and BAAV ITRs sequences claimed, along with the lack of disclosure regarding other sequences and variants, would require the skilled artisan to conclude that the single species of BAAV ITR and VP3 presented by the applicants is not sufficient to describe the claimed genus.

The specification does not provide any information on what amino acid or nucleic acid residues are necessary and sufficient for the disclosed BAAV ITR and VP3 properties relative to other AAV ITRs and VP3 proteins. The specification also provides no teachings on what amino acid sequence modifications, e.g. insertions, deletions and substitutions, would be permissible in a variant polypeptide that would improve or at least would not interfere with the biological activity or structural features necessary for the biological activity and stability of the protein. Furthermore, it is known in the art that even conservative amino acid substitutions can adversely affect proper folding and biological activity if amino acids that are critical for such functions are substituted, and the relationship between the sequence of a polypeptide and its tertiary structure is neither well understood nor predictable (see Ngo, in The Protein Folding Problem and Tertiary Structure Prediction, Merz et al. (eds.), Birkhauser Boston: Boston, MA, pp. 433 and 492-495, 1994). Rudinger (in Peptide Hormones, Parsons (ed.), University Park Press: Baltimore, MD, pp. 1-7, 1976) discloses that even for peptide hormones, which are much smaller than the instant BAAV VP3 protein, one cannot predict variant amino acid sequences for a biologically active polypeptide. Rather one must engage in “case to case painstaking experimental study” to

determine active variants (see page 7). Consequently, excessive trial and error experimentation would have been required to identify the necessary BAAV ITR and VP3 derivatives with the claimed properties since the amino- or nucleic acid sequence of such molecules could not be predicted - even were the activity known.

As set forth in In re Fisher, 166 USPQ 18 (CCPA 1970), compliance with 35 USC 112, first paragraph requires:

> that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved.

In Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016 (Fed. Cir. 1991), the court ruled that a claim to a large genus of possible genetic sequences encoding a protein with a particular function that needs to be determined subsequent to the construction of the genetic sequences may not find sufficient support under 35 USC 112, 1st ¶, if only a few of the sequences that meet the functional limitations of the claim are disclosed and if undue experimentation would be required of one skilled in the art for determining other genetic sequences embraced by the claim. This is the case here, where specification discloses only one putative functional sequence for each claimed component, SEQ ID NOs: 11 or 12, for a molecule having the necessary activity, and provides no guidance on determining which variants of SEQ ID NOs: 11 or 12 that would have such properties of SEQ ID NO: 11 or 12 such that would fall within the claimed scope.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Burkhart whose telephone number is (571)272-2915. The examiner can normally be reached on M-F 8AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael Burkhart/
Primary Examiner, Art Unit 1633